REMARKS

By the foregoing amendments, claims 1, 3-6, 10, and 13-90 are pending in this application. Claims 2, 7-9, 11, and 12 have been canceled without prejudice, and new claims 16-90 have been added.

Amended, independent claim 1 is directed to a method for early stage screening of prostate cancer, as described in the specification, for example, on page 25, lines 23-25 and page 58, lines 25-28. The method comprises assaying an expression product of a prostate cancer associated virus (PCAV), as described, for example, on page 7, lines 5-8. The PCAV expresses an RNA that hybridizes under high stringency hybridization conditions to a nucleotide sequence having SEQ ID NOS:7-10 or SEQ ID NOS:14-41 or to a complement of the nucleotide sequence, as described, for example, on page 42, lines 13-25. Dependent claims 4-6 have been amended to clarify that the RNA expression product comprises a nucleotide sequence corresponding to the recited DNA sequences, rather than the DNA sequences themselves. Dependent claim 10 has been amended to recite that the expression product is a polypeptide, as described, for example, on page 15, lines 25-26. New dependent claims 16-22 recite classes of PCAV polynucleotide and polypeptide expression products (*e.g.*, corresponding to the Gag or Pol domain of the PCAV), as well as expression products having particular polynucleotide and polypeptide sequences, as described, for example, on page 77, line 28 to page 78, line 8; page 37, lines 20-28; and Tables 6 and 8. New dependent claim 23 recites an increased expression product level as described, for example, on page 25, lines 17-19.

New independent claim 24 and dependent claims 32-34 are directed to a method for early stage screening of prostate cancer comprising assaying an expression product of a PCAV that expresses an RNA comprising a nucleotide sequence having levels of sequence identity to SEQ

ID NOS:7-10 or SEQ ID NOS:14-41, as described, for example, on page 41, line 25 to page 42, line 3 and page 64, lines 5-19. New dependent claims 25-31 and 35-39 are directed to embodiments which parallel those recited in dependent claims 3-6, 10, 16-21, and 23.

New independent claim 40 and dependent claims 48 and 49 are directed to a method for early stage screening of prostate cancer comprising assaying an expression product of a PCAV that expresses an RNA having levels of base pair mismatches, relative to SEQ ID NOS:7-10 or SEQ ID NOS:14-41, as described, for example, on page 41, lines 9-14. New dependent claims 41-47 and 50-53 are directed to embodiments which parallel those recited in dependent claims 3-6, 10, 16-21, and 23.

New independent claim 54 is directed to a method for early stage screening of prostate cancer comprising assaying an expression product of the HML-2 retrovirus HERV-K(CH), as described, for example, on page 37, lines 16-19. New dependent claims 55-65 are directed to embodiments which parallel those recited in dependent claims 3-6, 10, 16-20, and 23.

New independent claims 66, 75, and 84 are directed to further methods of screening for prostate cancer, comprising assaying the polynucleotide and polypeptide expression products described in the specification, as noted above. Dependent claims 67-74, 76-83, and 85-90 are directed to various embodiments which parallel those recited in one or more dependent claims 3-6, 10, 16-20, and 23.

The claim amendments and new claims add no new matter.

Claim Objections

Claim 1 is objected to because of the recitation of "gag or pol" rather than "Gag or Pol" according to art-recognized nomenclature. Also, claims 4-7 are objected to because, according to the Office Action, the recitation of "an RNA comprising SEQ ID NO:155 [claim 4] and SEQ ID NO:5 [claim 5] . . . does not further limit the base claim recitation 'wherein said expression product is an RNA corresponding to the Gag or Pol domain of said retrovirus'".

The above rejections are rendered moot by the deletion of the phrase "RNA corresponding to the gag or pol domain of said retrovirus" in claim 1. Also, all new claims referring to the Gag or Pol domain (*e.g.*, claim 17) have been written with "Gag" and "Pol" capitalized, as requested in the Office Action.

Reconsideration and withdrawal of the claim objections are respectfully requested.

The Rejections under 35 U.S.C. § 112, ¶ 1 (Written Description and Enablement)

Claims 1, 3-7, 10, and 13-15 have been rejected under 35 U.S.C. § 112, ¶ 1 as containing subject matter that was neither described nor enabled. The rejections of claim 7 have been rendered moot by the cancellation of this claim. Applicants respectfully traverse these rejections insofar as they apply to pending claims 1, 3-6, 10, and 13-15 as amended, as well as new claims 16-90.

With respect to the rejections based on written description, the Office Action contends, "Applicants have not disclosed the conserved structure in . . . or have compared structures between . . . all of the HML-2 retroviral genes as claimed." Likewise, regarding the rejections based on enablement, the Office Action faults the specification for "not provid[ing] guidance on the operative versus the inoperative HML-2 retroviral species."

To advance prosecution, pending claims 1, 3-6, 10, and 13-15 as amended (as well as new claims 16-90) are no longer directed to the genus of HML-2 retroviruses. Instead, these claims are directed the detection of expression products of the *particular* prostate cancer associated virus (PCAV) that expresses RNA corresponding to the DNA sequences SEQ ID NOS:7-10 and SEQ ID NOS:14-41 and closely homologous DNA sequences:

- In amended independent claim 1 and new independent claim 66 (as well as their dependent claims 3-6, 10, 13-23, and 67-74), the PCAV expresses, or the expression product comprises, "an RNA that hybridizes, under high stringency conditions" to the above DNA sequences,

- In new independent claims 24 and 75 (as well as their dependent claims 25-39 and 76-83), the PCAV expresses, or the expression product comprises, "an RNA comprising a nucleotide sequence corresponding to a DNA sequence having at least 90% sequence identity" to the above nucleotide sequences.

- In new independent claims 40 and 84 (as well as their dependent claims 41-53 and 85-90), the PCAV expresses, or the expression product comprises, "an RNA comprising a nucleotide sequence corresponding to a DNA sequence having at most about 5-15% base pair mismatches" relative to the above nucleotide sequences.

- In new independent claim 54 (as well as its dependent claims 55-65), the PCAV is HERV-K(CH).

Applicants have designated the particular PCAV having SEQ ID NOS:7-10 and SEQ ID NOS:14-41 as "HERV-K(CH)" in the specification. See page 37, lines 16-19. Sequences from HERV-K(CH) are shown in SEQ ID NOS:14-39, which have been deposited with the ATCC. See page 37, lines 20-21. Sequences from HERV-K(CH) additionally include SEQ ID NOS:40-41, which were found to be up-regulated in prostate cancer patient studies using a differential

expression assay. See page 74, line 26 to page 77, line 19. In fact, RNA expression products corresponding to all of the specific DNA sequences SEQ ID NOS:14-26, SEQ ID NO:40 and SEQ ID NO:41 (as recited in dependent claims 19, 20, 22, 31, 47, 52, 61, 64, and 72-74) were found to be upregulated in prostate cancer patients. See page 77, line 28 to page 79, line 5, as well as Tables 6 and 8.

As of the filing date, Applicants were thus in possession of at least the particular PCAV that expresses RNA corresponding to the DNA sequences SEQ ID NOS:7-10 and SEQ ID NOS:14-41, designated "HERV-K(CH)":

> The skilled person will be able to classify any further HERV as HERV-K(CH) or not based on sequence identity to these HERV-K(CH) polynucleotides . . . HERV-K(CH) is therefore a specific member of the HML-2 subgroup which can be used in the invention. . .

Page 37, line 20 to page 38, line 2.

Furthermore, Applicants' specification enables the claimed screening method, comprising detecting expression products of the particular PCAV, designated HERV-K(CH). In fact, *all 16 gene expression products* of this PCAV, corresponding to the DNA sequences SEQ ID NOS:14-26, SEQ ID NO:40 and SEQ ID NO:41, showed a significant degree of up-regulation in prostate tumor cells relative to normal cells. See Table 6.

Nevertheless, the pending claims are directed to screening methods that do not require a definitive diagnosis of cancer. Also, the Office Action's continued insistence on complete certainty with regard to whether "gene expression is indeed elevated in every prostate tumor sample" and for "the whole population of prostate cancer patients" is clearly well beyond what is required to meet the legal standard for enablement. To satisfy enablement, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and

use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

For the reasons given above, the specification both describes and enables the presently pending claims, directed to early stage cancer screening methods, comprising the detection of the expression products of a particular PCAV that Applicants have clearly found to be implicated in prostate cancer patients.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, ¶ 1 for lack of written description and enablement are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, all pending claims of this application are believed to be in condition for allowance. A written indication of the same is respectfully requested. This response is believed to completely address all of the substantive issues raised in the Final Office Action mailed March 22, 2007.

Please continue to direct all correspondence in this application to Novartis Vaccines and Diagnostics, Inc. (formerly Chiron Corporation), at the address provided for Customer No. 27476.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Date: August 22, 2007

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